

NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC™) GUIDELINE SYNTHESIS

SCREENING FOR THYROID DISEASE

Guidelines

- American College of Physicians-American Society of Internal Medicine (ACP-ASIM). [Screening for thyroid disease](#). Ann Intern Med 1998 Jul 15;129(2):141-3 [3 references] (guideline); Ann Intern Med 1998 Jul 15;129(2):144-58 [73 references] (background paper).
- American Thyroid Association (ATA). [Guidelines for detection of thyroid dysfunction](#). Arch Intern Med. 2000 Jun 12;160(11):1573-5 [23 references].

INTRODUCTION:

A direct comparison of ACP-ASIM and ATA recommendations on screening for thyroid disease is provided in the table below. Following the content comparison table and discussion, the areas of agreement and differences among the guidelines are identified. In general, the timing of the guideline with respect to available data is an important factor to consider when evaluating areas of differences among these guidelines. The rationale behind disparate recommendations that cannot be attributed to the evidence base available at the time of guideline development is also explored in the discussion of the areas of differences.

Abbreviations used in the text and tables follow:

- ACP-ASIM: American College of Physicians-American Society of Internal Medicine
- ATA: American Thyroid Association
- FT₄: serum free thyroxine
- FT₃: serum free triiodothyronine
- TSH: thyroid-stimulating hormone
- T₃: serum triiodothyronine

COMPARISON OF SCOPE AND CONTENT	
	OBJECTIVE AND SCOPE
ACP-ASIM (1997)	<ol style="list-style-type: none">To update recommendations on screening for thyroid disease in primary care setting.To review information of the benefits of screening with a sensitive thyroid-stimulating hormone (TSH) test for thyroid dysfunction i

	asymptomatic patients seeking primary care for other reasons.
ATA (2000)	To define the optimal approach to identify patients with thyroid dysfunction.
	TARGET POPULATION
ACP-ASIM (1997)	Adults
ATA (2000)	Adults
	INTENDED USERS
ACP-ASIM (1997)	Physicians
ATA (2000)	Physicians
	INTERVENTIONS AND PRACTICES CONSIDERED
ACP-ASIM (1997)	<p><i>Screening tests</i></p> <p>Measurement of:</p> <ul style="list-style-type: none"> • Serum thyroid-stimulating hormone (TSH) using a sensitive test <p><i>Other thyroid laboratory studies:</i></p> <ul style="list-style-type: none"> • Serum triiodothyronine (T₃) • Serum free thyroxine (FT₄) <p><i>Identification of patients who meet age and sex criteria for testing.</i></p>
ATA (2000)	<p><i>Screening tests</i></p> <p>Measurement of:</p> <ul style="list-style-type: none"> • Serum thyrotropin [thyroid-stimulating hormone (TSH)] <p><i>Other thyroid laboratory studies:</i></p> <ul style="list-style-type: none"> • Serum free thyroxine (FT₄) • Serum free triiodothyronine T₃ (FT₃)

	<p><i>Case finding:</i></p> <ul style="list-style-type: none"> • Assessment of signs and symptoms • Evaluation of personal and family medical histories • Laboratory studies
COMPARISON OF SCREENING RECOMMENDATIONS	
	Population Screening: Who Should Be Screened?
ACP-ASIM (1997)	<p>It is reasonable to screen women older than 50 years of age for unsuspected but symptomatic thyroid disease.</p> <p>Screening in women younger than 50 years of age and in men is not warranted because of the low prevalence of unsuspected but symptomatic thyroid dysfunction among these persons.</p>
ATA (2000)	<p>It is recommended that adults be screened for thyroid dysfunction by measurement of serum thyroid-stimulating hormone (TSH) concentration, beginning at age 35 years and every 5 years thereafter. The indication for screening is particularly compelling in women but it may also be justified in men as a relatively cost-effective measure in the context of the periodic health examination.</p> <p>Individuals with clinical manifestations potentially attributable to thyroid dysfunction, and those with risk factors for its development may require more frequent serum TSH testing.</p>
	Signs and Symptoms of Thyroid Dysfunction - Risk Factors That Justify Latent Testing
ACP-ASIM (1997)	<p>Older persons, in particular, may present with subtle, nonspecific signs and symptoms of thyroid dysfunction.</p> <p>Hyperthyroidism can cause weight loss, apathy, tremor, heat intolerance, and weakness. Hypothyroidism can cause muscle cramps, dry skin, intolerance to constipation, poor energy levels, fatigue, and mental slowness.</p> <p>The cause of these symptoms may be overlooked until an abnormal result on a screening test leads a physician to ask about them.</p> <p>Data show that selective testing based on signs and symptoms is neither as precise nor as effective as a screening test followed by a history and physical examination of selected patients.</p>
ATA (2000)	<p>A number of symptoms and signs are well-established manifestations of thyroid dysfunction.</p> <ul style="list-style-type: none"> • For hypothyroidism, these include fatigue, weight gain, cold intolerance, skin dryness, depression, dementia, muscle cramps and myalgias, edema, bradycardia, constipation, menstrual irregularity (especially menorrhagia)

	<p>infertility</p> <ul style="list-style-type: none"> For hyperthyroidism, these include fatigue, weight loss, heart intolerance, hyperhidrosis, nervousness, insomnia, tremor, muscle weakness, dyspnea, palpitations, tachycardia and atrial arrhythmias, hyperdefecation, and menstrual irregularity (especially hypermenorrhea) <p>Risk factors identifiable in personal history include (1) previous thyroid dysfunction; (2) goiter; (3) surgery or radiotherapy affecting the thyroid gland; (4) diabetes mellitus; (5) vitiligo; (6) pernicious anemia; (7) leukotrichia (prematurely gray hair); and (8) medications and other compounds, such as lithium carbonate and iodine-containing compounds.</p> <p>Risk factors identifiable in the family history include (1) thyroid disease, (2) pernicious anemia, (3) diabetes mellitus, and (4) primary adrenal insufficiency.</p> <p>Abnormal results in certain commonly obtained laboratory tests may also suggest thyroid dysfunction.</p> <ul style="list-style-type: none"> Findings of these tests for hypothyroidism may include (1) hypercholesterolemia, (2) hyponatremia, (3) anemia, (4) creatine phosphokinase and lactate dehydrogenase elevations, and (5) hyperprolactinemia. Findings of these tests for hyperthyroidism may include (1) hypercalcemia, (2) alkaline phosphatase elevation, and (3) hepatocellular enzyme elevation. These clinical and laboratory findings justify thyroid function testing, particularly if they are sustained for 2 weeks or more, occur in combination, have not been present previously during documented euthyroidism, or occur in individuals with an increased risk of thyroid disease.
	<p>Laboratory Screening Tests for Thyroid Disease</p> <ul style="list-style-type: none"> Preferred Test for Screening Other Thyroid Tests
ACP-ASIM (1997)	<p>The preferred screening method is a sensitive TSH test.</p> <p>A free thyroxine test should be done when the TSH level is undetectable or is 10 mIU/L or more. Patients who have an undetectable TSH level and an elevated free thyroxine level have overt hyperthyroidism. Patients who have a TSH level higher than 10 mIU/L and a low free thyroxine level have overt hypothyroidism.</p>
ATA (2000)	<p>Serum TSH measurement is the single most reliable test to diagnose all common thyroid disorders, both hypothyroidism and hyperthyroidism, particularly in the ambulatory setting.</p> <p>Measurement of serum free thyroxine (FT₄) and serum free triiodothyronine (FT₃) also be indicated in certain clinical circumstances:</p> <ul style="list-style-type: none"> Serum FT₄ concentration should be measured in addition to serum TSH when there is a suspicion of pituitary or hypothalamic disease. Serum FT₄ measurement and serum triiodothyronine (T₃) assay in patients with hyperthyroidism.

	<p>normal serum FT₄ level are indicated to further assess hyperthyroidism in with a serum TSH level < 0.1 mIU/L.</p> <ul style="list-style-type: none"> • When less sensitive TSH assays are the only ones available, a serum FT₄ or estimate and a total or free T₃ (FT₃) assay should be employed in addition to serum TSH concentration. • Two rare types of TSH-mediated hyperthyroidism (TSH-secreting pituitary adenomas and selective pituitary resistance to thyroid hormone) will be overlooked by serum TSH measurement alone; serum FT₄ and FT₃ concentrations should also be measured when these conditions are suspected. <p>Finally it is important to recognize that isolated abnormalities of the serum TSH concentration do not always connote sustained thyroid dysfunction and may be caused by other conditions and medications.</p>
	BENEFITS
ACP-ASIM (1997)	<p>Screening can detect symptomatic but unsuspected overt thyroid dysfunction. For women older than 50 years of age, 1 in 71 women screened could benefit from relief of symptoms.</p> <p>For screening to be cost-effective, the laboratory, clinic, or office should be equipped to identify patients who meet age and sex criteria for screening and to perform appropriate follow-up tests on the same serum sample without requiring a second venipuncture. In particular, the clinic must follow patients who have overt but clinically unrecognized disease because these patients derive the most definite benefit from treatment.</p>
ATA (2000)	Early detection of thyroid dysfunction is important because once diagnosed, hypothyroidism and hyperthyroidism can be treated before clinical complications ensue.
	HARMS
ACP-ASIM (1997)	Failure to screen younger women (i.e., women < 50 years of age) and men will put patients with subclinical or unrecognized thyroid disease at risk for complications. The benefits of screening must be balanced against the lack of strong evidence that treatment is effective in subclinical disease and the potential adverse effects of treatment.
ATA (2000)	Serum TSH concentration measurement in adults every 5 years may not be frequent enough for individuals at higher risk of developing thyroid dysfunction, possibly predisposing those individuals to undetected development of thyroid dysfunction. The benefits of screening (including false positive tests) were not discussed.

GUIDELINE CONTENT COMPARISON

The American College of Physicians-American Society of Internal Medicine (ACP-ASIM) and the American Thyroid Association (ATA) present recommendations for screening for thyroid disease and provide explicit reasoning behind their recommendations. ACP-ASIM also reviews the potential benefits and risks of treatment of overt and subclinical thyroid dysfunction.

Areas of Agreement

Recommended Laboratory Screening Tests

ACP-ASIM and ATA are in general agreement concerning the use of sensitive assays of serum thyroid-stimulating hormone (TSH) as the preferred laboratory screening strategy for detecting both hypothyroidism and hyperthyroidism.

Areas of Differences

Need for Routine Population Screening

Although ACP-ASIM and ATA both recommend routine screening in certain age and sex groups, ACP-ASIM recommends screening with thyroid function tests in women older than 50 years of age, while ATA recommends screening all adults beginning at age 35 years and every 5 years thereafter. The rationale for ACP-ASIM's recommendation is that well-designed prospective clinical and epidemiologic studies have found that 1 in 71 women over 50 years of age has unsuspected but symptomatic overt hypothyroidism or overt hyperthyroidism that will respond to treatment. ACP-ASIM does not recommend screening in younger women or in men because of the low prevalence of unsuspected overt thyroid dysfunction in these groups.

ATA states that thyroid dysfunction meets many criteria for a condition justifying population screening: (1) a substantial prevalence of various forms of thyroid dysfunction in the general population; (2) the well-established clinical consequences of overt hypothyroidism and hyperthyroidism, the possibility that mild (subclinical) hypothyroidism may progress to overt hypothyroidism, and may be associated with reversible hypercholesterolemia, reversible symptoms (in some patients), and cognitive dysfunction, and the association of mild (subclinical) hyperthyroidism with atrial fibrillation in older persons and reduced bone marrow density, particularly in postmenopausal women, and symptoms (e.g., palpitations) in some patients; (3) the safety, accuracy, and relatively low cost of the serum TSH assay; and (4) the availability of effective therapies for patients with hypothyroidism and hyperthyroidism. In addition, serum TSH measurements in adults every 5 years has been shown by decision analysis to have equivalent cost-effectiveness compared with other disease detection strategies, such as those for hypertension, breast cancer, and hypercholesterolemia. The cost-effectiveness of screening is more favorable in women and in the elderly and is strongly influenced by the cost of TSH measurement. Consequently, ATA recommends screening every adult beginning at age 35 years and every 5 years thereafter, the interval at which a periodic health examination has been advocated by the United States Preventive Services Task Force (USPSTF). ATA indicates that more frequent screening may be appropriate in individuals at higher risk of developing thyroid dysfunction.

Case Finding for Thyroid Dysfunction

ATA notes that abnormal results in certain commonly obtained laboratory tests suggest hypothyroidism or hyperthyroidism and, therefore, justify thyroid function testing. Findings of these tests for hypothyroidism may include (1) hypercholesterolemia, (2) hyponatremia, (3) anemia, (4) creatinine phosphokinase and lactate dehydrogenase elevations, and (5) hyperprolactinemia; and for hyperthyroidism (1) hypercalcemia, (2) alkaline

phosphatase elevation, and (3) hepatocellular enzyme elevation. Screening is particularly indicated if abnormalities persist for 2 weeks or more, occur in combination, have not been present previously during documented euthyroidism, or occur in individuals with increased risk of thyroid disease.

ATA also lists a number of risk factors for thyroid disease in the personal or family history that are not identified by ACP-ASIM. Risk factors identifiable in personal history include (1) previous thyroid dysfunction, (2) goiter, (3) surgery or radiotherapy affecting the thyroid gland, (4) diabetes mellitus, (5) vitiligo, (6) pernicious anemia, (7) leukotrichia (prematurely gray hair), and (8) medications and other compounds, such as lithium carbonate and iodine-containing compounds (e.g., amiodarone hydrochloride, radiocontrast agents, expectorants containing potassium iodide, and kelp). Risk factors identifiable in the family history include (1) thyroid disease, (2) pernicious anemia, (3) diabetes mellitus, and (4) primary adrenal insufficiency.

Other Thyroid Laboratory Screening Tests

Although ACP-ASIM and ATA recommend the measurement of serum TSH to accurately screen for certain types of thyroid disease (see areas of agreement, above), ACP-ASIM and ATA recommend additional thyroid function tests in certain distinct clinical situations. ACP-ASIM recommends that a free thyroxine test should be done when the TSH level is undetectable or is 10 mIU/L or more. ATA recommends measuring the serum free thyroxine (FT₄) concentration in addition to the serum TSH concentration when there is suspicion of pituitary or hypothalamic disease. ATA further recommends that serum free thyroxine (FT₄) measurement and serum triiodothyronine (T₃) assay in patients with a normal serum free thyroxine (FT₄) level are indicated to further assess patients with a serum TSH level less than 0.1 mIU/L.

ATA states that to diagnose hyperthyroidism accurately, TSH assay sensitivity must be 0.02 mIU/L or less, and recommends, when less sensitive TSH assays are available, a serum free thyroxine (FT₄) assay or estimate and a total or free T₃ (FT₃) assay be employed in addition to measurement of the serum TSH concentration. ATA also notes that there are two rare types of TSH-mediated hyperthyroidism, TSH-secreting pituitary adenoma and selective pituitary resistance to thyroid hormone that will be overlooked by serum TSH measurements alone and recommends that serum FT₃ and FT₄ concentrations should also be measured if these conditions are suspected. Finally, ATA notes that isolated abnormalities of TSH do not always indicate sustained thyroid dysfunction and may be caused by other conditions or medications that are delineated in the guideline.

This Synthesis was prepared by NGC on November 28, 2000. It was reviewed by the guideline developers on January 8, 2001. This Synthesis was updated most recently on February 20, 2002 following the withdrawal of the USPSTF guideline from the NGC Web site.

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